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PATENT

Attorney Docket No. A-71486-2
Dorsey File No. 463077-00240

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:

DESJARLAIS et al.

Serial No.: 10/611,363

Filing Date: July 1, 2003

For: *Novel Variants of RANKL Protein*

Examiner: To Be Assigned

Art Unit: 1647

CERTIFICATE OF MAILING

I hereby certify that this correspondence, including listed enclosures, is being deposited with sufficient postage with the United States Postal Service as First Class Mail in an envelope addressed to: Commissioner for Patents, P.O. BOX 1450, Alexandria, VA 22313-1450 on:

Date: August 13, 2004
Signed: Careyna Peralta
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**INFORMATION DISCLOSURE STATEMENT
AND
STATEMENT OF RELATEDNESS**

Commissioner for Patents
P. O. Box 1450
Alexandria, VA 22313-1450

Sir:

In satisfaction of the duty of disclosure under 37 C.F.R. § 1.56, and in accordance with the provisions of 37 C.F.R. §§ 1.97 and 1.98, Applicants wish to draw the attention of the U.S. Patent and Trademark Office to the references cited on the accompanying Form PTO/SB/08A-B, Substitute for form PTO 1449. This application is a continuation-in-part of the following related U.S. Application - Serial No. 10/338,785, filed January 6, 2003 (pending). The references cited on the accompanying form PTO/SB/08A-B, Substitute for form PTO-1449, not marked with an asterisk (*), were previously disclosed in the above-mentioned application and in accordance with 37 C.F.R. § 1.98(d), no copies of these references are enclosed.

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Further, in accordance with 1273 Off. Gaz. Pat. Off. 1, 8/5/2003, no copies of U.S. patents and U.S. published applications are enclosed. Copies of all other references are enclosed.

With respect to patent applications, the applicants point out their duty under M.P.E.P. §2001.06(b) to disclose relevant patent applications of which they are aware. To this end, the applicants draw the Examiner's attention to the following patent applications:

1. U.S.S.N. 10/888,748, filed July 9, 2004;
2. U.S.S.N. 10/611,399, filed July 1, 2003;
3. U.S.S.N. 10/336,242, filed January 3, 2003;
4. U.S.S.N. 10/794,751, filed March 5, 2004; and
5. U.S.S.N. 10/820,465, filed March 31, 2004.

None of the foregoing references is believed to disclose the invention as claimed.

Nothing herein shall constitute an admission concerning the contents of any of the cited references, nor shall the inclusion of a reference herein be considered an admission that the reference constitutes prior art against the invention claimed in the above-identified application. Submission of the present document shall not be construed as an admission that a search has been made or that better art does not exist.

As far as is known to the undersigned, this Information Disclosure Statement is being filed within three months of the filing date of a national application, within three months of the date of entry of the national state in an international application, or before the mailing date of a first Office Action on the merits as set forth in 37 C.F.R. § 1.97(b), and therefore no fee is required.

While no further fee is believed to be due, if this belief is in error, the Commissioner is authorized to charge any additional fees, including extension fees or other relief which may be

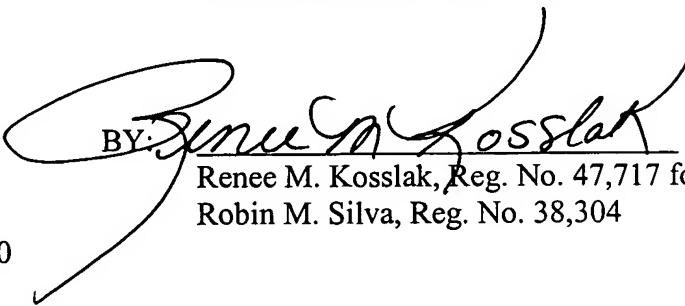
Serial No.: 10/611,373
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required, or credit any overpayment to Deposit Account No. 50-2319 (Our Order No. 463077-00240 (A-71486-2/RMS/RMK)).

Please direct any calls in connection with this application to the undersigned at (415) 781-1989.

Respectfully submitted,
DORSEY & WHITNEY LLP

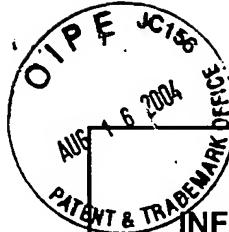
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Attachments:

Form PTO/SB/8A-B, Substitute for form PTO 1449
5 references



<p>Substitute for form 1449A/PTO (Modified)</p> <p>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</p> <p>(use as many sheets as necessary)</p>				Complete if Known	
				Application Number	10/611,363
				Filing Date	July 1, 2003
				First Named Inventor	DESJARLAIS, John R.
				Art Unit	1647
				Examiner Name	To Be Assigned
Sheet	1	of	6	Attorney Docket Number	A-71486-2

U.S. PATENT DOCUMENTS

Examiner Initials*	Cite No. ¹	U.S. Patent Document Number-Kind Code ² (if known)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
A1	5,843,678		12-01-1998	Boyle	
A2	6,017,729		01-25-2000	Anderson et al.	
A3 *	6,188,965 B1		02-13-2001	Mayo et al.	
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A23 *	2004/0043430 A1		03-04-2004	Dahiyat et al.	

FOREIGN PATENT DOCUMENTS

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B1 *	EP 0 974 111 B1		01-26-2000	California Institute of Technology		
B2 *	WO 98/47089 A1		10-22-1998	California Institute of Technology		
B3	WO 99/29865 A3		06-17-1999	The Rockefeller University		
B4	WO 00/15807 A1		03-23-2000	M & E Biotech		
B5 *	WO 00/23564 A2		04-27-2000	Xencor, Inc.		

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¹Applicant's unique citation designation number (optional). ² See Kinds Codes of USPTO Patent Documents at www.uspto.gov or MPEP 901.04. ³ Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). ⁴ For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. ⁵ Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. ⁶ Applicant is to place a check mark here if English Language Translation is attached.

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the complete application form to the USPTO. Time will vary depending on the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

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<p>Substitute for form 1449A/PTO (Modified)</p> <p>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</p> <p>(use as many sheets as necessary)</p>				Complete if Known	
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B6	*	WO 01/59066 A2, A3	08-16-2001	Xencor, Inc.		
B7	*	WO 03/014325 A2, A3	02-20-2003	Xencor		
B8		WO 03/033663 A2	04-24-2003	Barnes-Jewish Hospital		
B9		WO 03/033664 A2	04-24-2003	Barnes-Jewish Hospital		

NON PATENT LITERATURE DOCUMENTS							
Examiner Initials*	Cite No.	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.					T ⁶
	C1	ADLER, S.H., and TURKA L.A., "Immunotherapy as a means to induce transplantation tolerance," <i>Curr Opin Immunol</i> , 2002 Oct, 14(5):660-5.					
	C2	ALATALO S.L., et al., "Rapid Screening Method for Osteoclast Differentiation in Vitro That Measures Tartrate-resistant Acid Phosphatase 5b Activity Secreted into the Culture Medium," <i>Clin Chem</i> , 2000 Nov, 46(11):1751-4.					
	C3	ANDERSON DM, et al., "A homologue of the TNF receptor and its ligand enhance T-cell growth and dendritic-cell function," <i>Nature</i> , 1997 Nov 13, 390(6656):175-9.					
	C4	ARRON JR, and CHOI Y, "Bone versus immune system," <i>Nature</i> , 2000 Nov 30, 408(6812):535-6.					
	C5	ATKINS GJ, et al., "Osteoprotegerin inhibits osteoclast formation and bone resorbing activity in giant cell tumors of bone," <i>Bone</i> , 2001 Apr, 28(4):370-7.					
	C6	BACHMANN MF, and KOPF M., "Balancing protective immunity and immunopathology," <i>Curr Opin Immunol</i> , 2002 Aug, 14(4):413-9.					
	C7	BIANCHI L, et al., "A cluster region of AP-1 responsive elements is required for transcriptional activity of mouse ODC gene by hepatocyte growth factor," <i>Arch Biochem Biophys</i> , 2002 May 1, 401(1):115-23.					
	C8	BODMER JL, et al., "The molecular architecture of the TNF superfamily," <i>Trends Biochem Sci</i> , 2002 Jan, 27(1):19-26.					
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	C11	COMPSTON JE., "Bone marrow and bone: a functional unit," <i>J Endocrinol.</i> , 2002 Jun, 173(3):387-94.					
	C12	CUROTT DE LAFAILLE MA, and LAFAILLE JJ., "CD4(+) regulatory T cells in autoimmunity and allergy," <i>Curr Opin Immunol</i> , 2002 Dec, 14(6):771-8.					
	C13	DARNAY BG, et al., "Characterization of the intracellular domain of receptor activator of NF-kappaB (RANK). Interaction with tumor necrosis factor receptor-associated factors and activation of NF-kappaB and c-Jun N-terminal kinase," <i>J Biol Chem.</i> , 1998 Aug 7, 273(32):20551-5.					

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C14		DEYAMA Y, et al., "Histamine stimulates production of osteoclast differentiation factor/receptor activator of nuclear factor-kappaB ligand by osteoblasts," <i>Biochem Biophys Res Commun.</i> , 2002 Oct 25, 298(2):240-6.	
C15		FATA JE, et al., "The osteoclast differentiation factor osteoprotegerin-ligand is essential for mammary gland development," <i>Cell.</i> , 2000 Sep 29, 103(1):41-50.	
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C18		GOOD CR, et al., "Immunohistochemical study of receptor activator of nuclear factor kappa-B ligand (RANK-L) in human osteolytic bone tumors," <i>J Surg Oncol.</i> , 2002 Mar, 79(3):174-9.	
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C21		GRAVALLESE EM, et al., "The role of TNF-receptor family members and other TRAF-dependent receptors in bone resorption," <i>Arthritis Res.</i> , 2001, 3(1):6-12.	
C22		HOFBAUER LC, et al., "Interleukin-1beta and tumor necrosis factor-alpha, but not interleukin-6, stimulate osteoprotegerin ligand gene expression in human osteoblastic cells," <i>Bone</i> , 1999 Sep, 25(3):255-9.	
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C25		HOTOKEZAKA H, et al., "U0126 and PD98059, specific inhibitors of MEK, accelerate differentiation of RAW264.7 cells into osteoclast-like cells," <i>J Biol Chem.</i> , 2002 Dec 6, 277(49):47366-72.	
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C27		HUBER DM, et al., "Androgens suppress osteoclast formation induced by RANKL and macrophage-colony stimulating factor," <i>Endocrinology</i> , 2001 Sep, 142(9):3800-8.	
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C31		KITAZAWA R, and KITAZAWA S., "Vitamin D ₃ augments osteoclastogenesis via vitamin D-responsive element of mouse RANKL gene promoter," <i>Biochem Biophys Res Commun.</i> , 2002 Jan 18, 290(2):650-5.	
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C33		KONG YY, et al., "Activated T cells regulate bone loss and joint destruction in adjuvant arthritis through osteoprotegerin ligand," <i>Nature</i> , 1999 Nov 18, 402(6759):304-9.	

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	C34	LACEY DL, et al., "Osteoprotegerin ligand is a cytokine that regulates osteoclast differentiation and activation," <i>Cell</i> , 1998 Apr 17, 93(2):165-76.			
	C35	LAM J, et al., "TNF-alpha induces osteoclastogenesis by direct stimulation of macrophages exposed to permissive levels of RANK ligand," <i>J Clin Invest.</i> , 2000 Dec, 106(12):1481-8.			
	C36	LAM J, et al., "Crystal structure of the TRANCE/RANKL cytokine reveals determinants of receptor-ligand specificity," <i>J Clin Invest.</i> , 2001 Oct, 108(7):971-9.			
	C37	LARK MW, and JAMES IE, "Novel bone antiresorptive approaches," <i>Curr Opin Pharmacol.</i> , 2002 Jun, 2(3):330-7.			
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	C42	LUM L, et al., "Evidence for a role of a tumor necrosis factor-alpha (TNF-alpha)-converting enzyme-like protease in shedding of TRANCE, a TNF family member involved in osteoclastogenesis and dendritic cell survival," <i>J Biol Chem.</i> , 1999 May 7, 274(19):13613-8.			
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	C44	MATSUZAKI K, et al., "Osteoclast differentiation factor (ODF) induces osteoclast-like cell formation in human peripheral blood mononuclear cell cultures," <i>Biochem Biophys Res Commun.</i> , 1998 May 8, 246(1):199-204.			
	C45	McHUGH KP, et al., "Mice lacking beta3 integrins are osteosclerotic because of dysfunctional osteoclasts," <i>J Clin Invest.</i> , 2000 Feb, 105(4):433-40.			
	C46	MENAA C, et al., "Enhanced RANK ligand expression and responsivity of bone marrow cells in Paget's disease of bone," <i>J Clin Invest.</i> , 2000 Jun, 105(12):1833-8.			
	C47	NAKAGAWA N, et al., "RANK is the essential signaling receptor for osteoclast differentiation factor in osteoclastogenesis," <i>Biochem Biophys Res Commun.</i> , 1998 Dec 18, 253(2):395-400.			
	C48	NAKASHIMA T, et al., "Protein expression and functional difference of membrane-bound and soluble receptor activator of NF-kappaB ligand: modulation of the expression by osteotropic factors and cytokines," <i>Biochem Biophys Res Commun.</i> , 2000 Sep 7, 275(3):768-75.			
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	C51	QUINN JM, et al., "A combination of osteoclast differentiation factor and macrophage-colony stimulating factor is sufficient for both human and mouse osteoclast formation in vitro," <i>Endocrinology</i> , 1998 Oct, 139(10):4424-7.			
	C52	QUINN JM, et al., "The generation of highly enriched osteoclast-lineage cell populations," <i>Bone</i> , 2002 Jan, 30(1):164-70.			

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				Application Number	10/611,363
				Filing Date	July 1, 2003
				First Named Inventor	DESJARLAIS, John R.
				Art Unit	1647
				Examiner Name	To Be Assigned
Sheet	5	of	6	Attorney Docket Number	A-71486-2

NON PATENT LITERATURE DOCUMENTS

Examiner Initials*	Cite No.	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T ⁶
	C53	RODAN GA, and Martin TJ, "Therapeutic approaches to bone diseases," <i>Science</i> , 2000 Sep 1, 289(5484):1508-14.	
	C54	ROMAS E, et al., "Involvement of receptor activator of NF κ B ligand and tumor necrosis factor-alpha in bone destruction in rheumatoid arthritis," <i>Bone</i> , 2002 Feb, 30(2):340-6.	
	C55	SABOKBAR A, et al., "Two distinct cellular mechanisms of osteoclast formation and bone resorption in periprosthetic osteolysis," <i>J Orthop Res.</i> , 2003 Jan, 21(1):73-80.	
	C56	SAIDENBERG KERMANAC'H N, et al., "Osteoprotegerin and inflammation," <i>Eur Cytokine Netw.</i> , 2002 Apr-Jun, 13(2):144-53.	
	C57	SCHLONDORFF J, et al., "Biochemical and pharmacological criteria define two shedding activities for TRANCE/OPGL that are distinct from the tumor necrosis factor alpha convertase," <i>J Biol Chem.</i> , 2001 May 4, 276(18):14665-74.	
	C58	SCHOPPET M, et al., "RANK ligand and osteoprotegerin: paracrine regulators of bone metabolism and vascular function," <i>Arterioscler Thromb Vasc Biol.</i> , 2002 Apr 1, 22(4):549-53.	
	C59	SENIOR K., "Vaccinating against bone destruction," <i>Drug Discov Today</i> , 2001 Dec 15, 6(24):1243-1244.	
	C60	SHEVDE NK, et al., "Estrogens suppress RANK ligand-induced osteoclast differentiation via a stromal cell independent mechanism involving c-Jun repression," <i>Proc Natl Acad Sci U S A</i> , 2000 Jul 5, 97(14):7829-34.	
	C61	SRIVASTAVA S, et al., "Estrogen decreases osteoclast formation by down-regulating receptor activator of NF- κ B ligand (RANKL)-induced JNK activation," <i>J Biol Chem.</i> , 2001 Mar 23, 276(12):8836-40.	
	C62	SUDA T, et al., "Modulation of osteoclast differentiation and function by the new members of the tumor necrosis factor receptor and ligand families," <i>Endocr Rev.</i> , 1999 Jun, 20(3):345-57.	
	C63	TAKAHASHI N, et al., "A new member of tumor necrosis factor ligand family, ODF/OPGL/TRANCE/RANKL, regulates osteoclast differentiation and function," <i>Biochem Biophys Res Commun.</i> , 1999 Mar 24, 256(3):449-55.	
	C64	TAKAYANAGI H, et al., "RANKL maintains bone homeostasis through c-Fos-dependent induction of interferon-beta," <i>Nature</i> , 2002 Apr 18, 416(6882):744-9.	
	C65	TAKAYANAGI H, et al., "Signaling crosstalk between RANKL and interferons in osteoclast differentiation," <i>Arthritis Res.</i> , 2002, 4(Suppl 3):S227-32.	
	C66	TEITELBAUM SL., "Bone resorption by osteoclasts," <i>Science</i> , 2000 Sep 1, 289(5484):1504-8.	
	C67	THEILL LE, et al., "RANK-L and RANK: T cells, bone loss, and mammalian evolution," <i>Annu Rev Immunol.</i> , 2002, 20:795-823.	
	C68	TSUDA E, et al., "Isolation of a novel cytokine from human fibroblasts that specifically inhibits osteoclastogenesis," <i>Biochem Biophys Res Commun.</i> , 1997 May 8, 234(1):137-42.	
	C69	UDAGAWA N, et al., "Origin of osteoclasts: mature monocytes and macrophages are capable of differentiating into osteoclasts under a suitable microenvironment prepared by bone marrow-derived stromal cells," <i>Proc Natl Acad Sci U S A</i> , 1990 Sep, 87(18):7260-4.	
	C70	VANDERKERKEN K, et al., "Recombinant osteoprotegerin decreases tumor burden and increases survival in a murine model of multiple myeloma," <i>Cancer Res.</i> , 2003 Jan 15, 63(2):267-9.	
	C71	WEI S, et al., "Receptor activator of nuclear factor- κ B ligand activates nuclear factor- κ B in osteoclast precursors," <i>Endocrinology</i> , 2001 Mar, 142(3):1290-5.	
	C72	WEKERLE T, et al., "Mechanisms of transplant tolerance induction using costimulatory blockade," <i>Curr Opin Immunol.</i> , 2002 Oct, 14(5):592-600.	

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	C73	WILLARD D, et al., "Expression, purification, and characterization of the human receptor activator of NF-kappaB ligand (RANKL) extracellular domain," <i>Protein Expr Purif.</i> , 2000 Oct, 20(1):48-57.			
	C74	WONG BR, et al., "TRANCE is a novel ligand of the tumor necrosis factor receptor family that activates c-Jun N-terminal kinase in T cells," <i>J Biol Chem.</i> , 1997 Oct 3, 272(40):25190-4.			
	C75	WUYTS W, et al., "Evaluation of the role of RANK and OPG genes in Paget's disease of bone," <i>Bone</i> , 2001 Jan, 28(1):104-7.			
	C76	YAMAGISHI T, et al., "Reciprocal control of expression of mRNAs for osteoclast differentiation factor and OPG in osteogenic stromal cells by genistein: evidence for the involvement of topoisomerase II in osteoclastogenesis," <i>Endocrinology</i> , 2001 Aug, 142(8):3632-7.			
	C77	YASUDA H, et al., "Osteoclast differentiation factor is a ligand for osteoprotegerin/osteoclastogenesis-inhibitory factor and is identical to TRANCE/RANKL," <i>Proc Natl Acad Sci U S A</i> , 1998 Mar 31, 95(7):3597-602.			

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